Reviewer's report

Title: Ability of Ambulatory ECG-based T-wave Alternans to Modify Risk Assessment of Cardiac Events

Version: 2
Date: 30 October 2014
Reviewer: Richard Verrier

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COMPULSORY REVISIONS:

1. AECG-based TWA is described as “not well established” (abstract, line 4) or “a promising candidate” (background, line 53). However, historically, TWA has been noted on AECGs to indicate an ominous finding, for example in the setting of proarrhythmia, and it has long been appreciated as an indicator of the Brugada and long QT syndromes. Thus, these statements should be modified. Recently, it has become possible to measure TWA amplitude precisely.

2. The authors should consider for possible inclusion in this metaanalysis the study by Ren L-N, Fang X-H, Ren L-D, et al. Ambulatory ECG-based T-wave alternans and heart rate turbulence can predict cardiac mortality in patients with myocardial infarction with or without diabetes mellitus. Cardiovasc Diabetol 2012; 11:104-111.

3. Background, line 56; discussion lines 165 to 180: When spectral method studies are described, the term “spectral method” should be used not “exercise-based.” By the way, MMA was used during routine, symptom limited exercise testing in the Finnish Cardiovascular Study (FINCAVAS) in nearly 3600 consecutive patients (Leino et al 2011; 8:385–390).

1. Background, line 60: The study by Monasterio was not negative.

2. Background, line 60: The study by Arisha et al (2013) was not negative, as TWA produced an ROC = 0.64 for SCD or life-threatening ventricular arrhythmias within 6 months. The Arisha study should be included in the tables.

3. Methods, line 85: The authors use the term study and trial interchangeably. The term trial is applied only when an intervention has taken place.

4. Statements regarding “no unified classification” and the necessity to “standardize the methodology” regarding “cut off values” in discussion, lines 201-208, should be changed to indicate that there are two standard cutpoints for MMA: 47 microvolts, which indicates “abnormal” and 60 microvolts which indicates “severely abnormal” test results, as described in the TWA consensus paper (your reference 1).

5. It should be appreciated that the positive predictive value varies among study populations and is less important than providing an opportunity for physicians to
use TWA magnitude in risk assessment, similarly to how other test results are presented, such as blood pressure.

MINOR ESSENTIAL REVISIONS

The authorship of the article by Hou et al 2013 (reference 19—now “Yu et al”) is mislabeled potentially because of English language listing.

DISCRETIONARY REVISIONS

In the abstract and background, a comment could be made indicating that ambulatory ECG (AECG)-based TWA is an important alternative platform to exercise for risk stratification of cardiac events. The TWA consensus guideline, your first reference, should be cited in this context.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I am an inventor of the Modified Moving Average method for T-wave alternans analysis and receive post-market royalty from sales of this software by GE Healthcare.